AMENDMENT

In the Claims

Please amend claims 2, 4-10, 12-17, 21-27, 29, and 31 as set forth below and cancel claims 1 and 34-37. Please add new claim 38. Upon entry of the present amendments and new claim, the status of the claims will be as set forth below in the listing of claims. This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims

1. (Cancelled).

2. (Currently Amended) The method of claim ~~1~~ 38, further comprising correlating the information with information ~~regarding source of~~ about a patient from which the sample is obtained.

3. (Original) The method of claim 2, wherein the capture probe is a primary antibody that binds specifically to the protein in the complex.

4. (Currently Amended) The method of claim ~~1~~ 38, wherein the ~~a~~ Raman-active probe construct comprises a secondary antibody as probe and one or more Raman tags.

5. (Currently Amended) The method of claim 4, wherein the Raman-active probe construct is a composite organic-inorganic nanoparticle (COIN) ~~COIN~~ with a unique surface enhanced Raman spectroscopy (SERS) ~~SERS~~ signature and the Raman spectrum detected is a SERS spectrum.

6. (Currently Amended) The method of claim ~~1~~ 38, wherein the proteins are solubilized in an aqueous solution or hydrophilic solvent prior to the separation.

7. (Currently Amended) The method of claim ~~1~~ 38, further comprising ~~denaturing~~ contacting the proteins in the sample with a denaturing agent prior to the separation to obtain denatured proteins.

8. (Currently Amended) The method of claim 7, wherein the denaturing agent is selected from a reducing agent, a surfactant, a chaotropic salt, and a combination thereof ~~is used to denature the proteins~~.

9. (Currently Amended) The method of claim 8, wherein the denatured proteins are dried on the substrate prior to the detection of signals.

10. (Currently Amended) The method of claim ~~1~~ 38, wherein the substrate is coated with one or more organic or inorganic materials prior to immobilization of the proteins thereon

11. (Original) The method of claim 10, wherein the separated proteins are deposited at the discrete locations on the solid substrate by a procedure selected from contact writing, contact spotting, liquid spraying, and dry particle spraying.

12. (Currently Amended) The method of claim ~~1~~ 38, wherein the separated proteins are deposited without denaturing using wet electrospray deposition.

13. (Currently Amended) The method of claim ~~1~~ 38, wherein the substrate is aluminum.

14. (Currently Amended) The method of claim ~~1~~ 38, wherein the substrate is comprised of a plurality of the discrete locations on a flat plate.

15. (Currently Amended) The method of claim ~~1~~ 38 or 14, wherein the detecting is automated to accomplish high throughput scanning at ~~sequential~~ a plurality of discrete protein enriched locations.

16. (Currently Amended) The method of claim ~~1~~ 38, wherein the discrete locations on the substrate comprise a material selected from gold, silver, copper, and aluminum metals, glass, silicon, and ceramic materials.

17. (Currently Amended) The method of claim ~~1~~ 38, further comprising contacting the proteins at the discrete protein enriched locations with silver nanoparticles, in individual or aggregate forms.

18. (Original) The method of claim 17, further comprising contacting the nanoparticles with at least one chemical enhancer salt.

19. (Original) The method of claim 18, wherein the chemical enhancer salt is LiCl.

20. (Original) The method of claim 17 or 18, wherein the Raman spectra are SERS spectra.

21. (Currently Amended) The method of claim ~~1~~ 38 or 17, further comprising collecting the Raman spectra or SERS spectra from the discrete protein enriched locations to compile a protein profile of the sample.

22. (Currently Amended) The method of claim 21, wherein the collection is automated to accomplish high-throughput SERS spectra screening of the discrete protein enriched locations.

23. (Currently Amended) The method of claim ~~1~~ 38, wherein the ~~relation between SERS~~ Raman spectra and ~~sample~~ locations of the proteins on the solid substrate or within the at least one stream of flowing liquid are recorded and correlated.

24. (Currently Amended) The method of claim ~~1~~ 38 or 22, wherein the spectrum contains information regarding a protein characteristic selected from a chemical bond, residue composition, residue structure, relative positions of residues, identity of the protein, and combinations thereof.

25. (Currently Amended) The method of claim ~~1~~ 38, wherein maintaining the separated proteins ~~are maintained~~ in a separated state ~~by sequentially introducing the separated proteins or fragments into the flowing stream to form the discrete locations~~ comprises depositing each fraction at a discrete location within at least one stream of flowing liquid in a microfluidic system to create a plurality of discrete protein enriched locations.

26. (Currently Amended) The method of claim 25, further comprising mixing the stream of flowing liquid comprising the separated proteins with a stream of flowing liquid comprising metal colloids by combining the streams under conditions suitable for contacting the separated proteins with the metal colloids ~~formation of SERS-active nanoparticles~~ and the detection is SERS detection.

27. (Currently Amended) The method of claim ~~1~~ 38, further comprising analyzing the separated proteins by mass spectroscopy to identify one or more functional groups contained within a separated protein or fragment thereof.

28. (Original) The method of claim 27, further comprising compiling data obtained from the Raman spectra or SERS spectra with data obtained from the mass spectroscopy.

29. (Currently Amended) The method of claim ~~1~~ 38 or 28, wherein the sample is a patient sample.

30. (Original) The method of claim 29, wherein the patient sample is a body fluid selected from urine, blood, plasma, serum, saliva, semen, stool, sputum, cerebral spinal fluid, tears, and mucus.

31. (Currently Amended) The method of claim ~~1~~ 38 further comprising creating a protein profile of the sample based on data obtained from the Raman spectra and/or the SERS spectra.

32. (Original) The method of claim 31, further comprising repeating the method using a variety of different patient samples to create a protein library containing a plurality of different protein profiles.

33. (Original) The method of claim 32 further comprising comparing the protein profile of the sample with one or more protein profiles of the library to detect a difference, wherein the difference is indicative of a disease in the patient.

Claim 34-37. (Canceled)

38. (New) A method for analyzing protein content of a complex biological sample, comprising:

a) chromatographically separating proteins and protein fragments in the sample into a plurality of fractions, each fraction containing an individual protein or protein fragment;

b) depositing each fraction at a discrete location on a solid substrate or within at least one stream of flowing liquid in a microfluidic system to create a plurality of discrete protein enriched locations, thereby maintaining the chromatographically separated proteins and protein fragments in a separated state;

c) contacting the separated proteins deposited at the plurality of discrete protein enriched locations with probes under conditions suitable to form a capture probe/protein complex at one or more of the discrete protein enriched locations;

d) contacting the complexes with a Raman-active probe construct that binds to the protein or the complex; and

e) detecting Raman spectra produced by the probe construct/protein complexes at the plurality of discrete protein enriched locations, wherein a Raman spectrum at a discrete protein enriched location provides information about the chemical composition of a protein deposited at the corresponding discrete protein enriched location, thereby analyzing the protein content of a complex biological sample.